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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/636,387	08/09/2000	John R Stuelpnagel	A-67616-2/DJB/RMS/DCF	5553

7590 10/17/2002

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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	15

DATE MAILED: 10/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/636,387	STUELPNAGEL ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-54 and 61-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-54 and 61-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This action is in response to papers filed 22 July 2002 in Paper No. 14 in which claims 49 and 61 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action of Paper No. 13 dated 16 April 2002 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Currently claims 49-54 and 61-75 are pending.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 49-54, 61-63, 65-69 and 71-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al. (U.S. Patent No. 6,327,410 B1, filed 11 September 1998) in view of Brenner (U.S. Patent No. 5,863,722, filed 7 June 1995) and in view of the definitions of Morris ed. (Academic Press Dictionary of Science and Technology, Academic Press, 1992, page 821).

Regarding Claim 49, Walt et al. teach a method of determining the presence of a target analyte in a sample comprising: acquiring a first data image of a random array composition

comprising: a substrate with a surface comprising discrete sites; a population of microspheres comprising at least a first and a second sub-population each comprising a bioactive agent; and a fiducial (i.e. marker bead, Column 19, lines 2-5) wherein said microspheres are randomly distributed on said surface such that said discrete sites contain microspheres; using the fiducial to register said first data image to create a registered first data image; contacting said random array with said sample; acquiring a second data image from said array with said sample; using the fiducial to register said second data image to create a registered second data image; and comparing said first and said second registered data images to determine the presence or absence of said target analyte (Column 18, line 59-Column 19, line 62 and Claims 17-21) wherein additional, non-optical signature encoding, is used e.g. size, shape and/or dimension of the microspheres and/or optical fibers (Column 19, lines 6-30) but they do not specifically teach at least one microsphere subpopulation does not have an optical signature. However, microspheres without optical signatures were well known in the art at the time the claimed invention was made as taught by Brenner et al. who teach a similar array composition comprising: a substrate with a surface comprising discrete sites; and a population of microspheres comprising at least a first and second subpopulation wherein each subpopulation comprises a bioactive agent wherein the microspheres are distributed on said surface wherein the microsphere does not comprise an optical signature and wherein microspheres size and shape are selected based on experimental design (Column 9, lines 62-65; Column 19, line 20-49; and Column 21, line 15-Column 22, line 61). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the microspheres not having an optical signature as taught by Brenner et al and the non-optical signature encoding taught by Walt et al to the microsphere compositions of Walt et al and to provide at least one subpopulation of microsphere without an optical signature thereby eliminating the need to provide optical signatures on all the microspheres for the obvious benefits of simplicity. One skilled in the art would have been further motivated to modify the

microspheres of Walt et al by replacing the optical signature microspheres of one subpopulation with non-labeled microspheres to be used to detect labeled targets wherein only microspheres bound to labeled targets are detected for the obvious benefits of target-specific detection.

Regarding Claim 50, Walt et al teach the method wherein the array comprises a fiber optic bundle and the registration of the first data image utilizes a fiducial fiber (Column 19, lines 2-53).

Regarding Claim 51, Walt et al teach the method wherein the array comprises microspheres and the registration of the first data image utilizes a fiducial microsphere i.e. marker bead (Column 19, lines 2-53).

Regarding Claim 52, Walt et al teach the method wherein the registration utilizes a fiducial template i.e. subarray bundle (Column 18, lines 59-66).

Regarding Claim 53, Walt et al. teach the method wherein the bioactive agents are proteins (Column 7, lines 55-61).

Regarding Claim 54, Walt et al. teach the method wherein the bioactive agents are nucleic acids (Column 7, lines 55-61).

Regarding Claim 61, Walt et al. teach a method of determining the presence of a target analyte in a sample comprising: providing a first data image of a random array comprising: a substrate with a surface comprising discrete sites; a population of microspheres comprising at least a first and a second sub-population each comprising a bioactive agent; and a fiducial (i.e. marker bead, Column 19, lines 2-5) wherein said microspheres are randomly distributed on said surface such that said discrete sites contain microspheres; contacting said random array with said sample; acquiring a second data image from said array with said sample; using the fiducial to register said second data image to create a registered second data image; and comparing said first and said second registered data images to determine the presence or absence of said target analyte (Column 18, line 59-Column 19, line 62 and Claims 17-21)

wherein additional, non-optical signature encoding, is used e.g. size, shape and/or dimension of the microspheres and/or optical fibers (Column 19, lines 6-30) but they do not specifically teach at least one microsphere subpopulation does not have an optical signature. However, microspheres without optical signatures were well known in the art at the time the claimed invention was made as taught by Brenner et al. who teach a similar array composition comprising: a substrate with a surface comprising discrete sites; and a population of microspheres comprising at least a first and second subpopulation wherein each subpopulation comprises a bioactive agent wherein the microspheres are distributed on said surface wherein the microsphere does not comprise an optical signature and wherein microspheres size and shape are selected based on experimental design (Column 9, lines 62-65; Column 19, line 20-49; and Column 21, line 15-Column 22, line 61). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the microspheres not having an optical signature as taught by Brenner et al and the non-optical signature encoding taught by Walt et al to the microsphere compositions of Walt et al and to provide at least one subpopulation of microsphere without an optical signature thereby eliminating the need to provide optical signatures on all the microspheres for the obvious benefits of simplicity. One skilled in the art would have been further motivated to modify the microspheres of Walt et al by replacing the optical signature microspheres of one subpopulation with non-labeled microspheres to be used to detect labeled targets wherein only microspheres bound to labeled targets are detected for the obvious benefits of target-specific detection.

Regarding Claim 62, Walt et al. teach the method of Claim 49 wherein the substrate is selected from the group consisting of glass and plastic i.e. optical fibers (Column 5, lines 57-60) which are comprised of glass or plastic as defined by Morris ed. (page 821).

Regarding Claim 63, Walt et al teach the method wherein the registration utilizes a fiducial edge i.e. subarray bundle (Column 18, lines 59-66).

Regarding Claim 65, Walt et al. teach the method of Claims 53 and 54 wherein the substrate is selected form the group consisting of glass and plastic i.e. optical fibers (Column 5, lines 57-60) which are comprised of glass or plastic as defined by Morris ed. (page 821).

Regarding Claim 66, Walt et al. teach the method of Claims 49 and 62 wherein each sub-population comprises a unique optical signature (Column 13, lines 8-24).

Regarding Claim 67, Walt et al. teach the method wherein the said unique optical signature is a bleed-through signature i.e. the signal is obtained from multiple wavelengths (Column 14, line 17-67).

Regarding Claim 68, Walt et al. teach the method of Claims 49 and 62 wherein each sub-population comprises an identifier binding ligand that will bind a decoder binding ligand such that the identification of the bioactive agent can be elucidated i.e. enzyme and substrate whereby the enzyme is identified in the presence of the substrate (Column 20, line 51-Column 21, line 6).

Regarding Claim 69, Walt et al teach the array comprises at least three fiducial and each is a fiducial fiber i.e. a unique tag for each of 100 different subarrays (Column 18, line 59-Column 19, line 5).

Regarding Claim 71, Walt et al teach the array wherein the fiducial fibers have a different color i.e. unique tag (Column 18, lines 59-66).

Regarding Claim 72, Walt et al teach the array wherein the registration utilizes at least three fiducial and each of said fiducials is a microsphere i.e. marker beads which identify each of 100 subarrays (Column 18, line 57-column 19, line 5).

Regarding Claim 73, Walt et al teach the fiducials have different sizes (Column 19, lines 6-30).

Regarding Claim 74, Walt et al teach the array wherein the fiducial fibers have a different color i.e. unique tag (Column 18, lines 59-66).

4. Claims 64, 70 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walt et al. (U.S. Patent No. 6,327,410, filed 11 September 1998) in view of Brenner (U.S. Patent No. 5,863,722, filed 7 June 1995) and in view of the definitions of Morris ed. (Academic Press Dictionary of Science and Technology, Academic Press, 1992, page 821) as applied to Claims 49 and 61 above and further in view of Augenlicht (U.S. Patent No. 4,981,783, filed 16 April 1986)

Regarding Claim 64, Walt et al. teach a method of determining the presence of a target analyte in a sample comprising: acquiring a first data image of a random array composition comprising: a substrate with a surface comprising discrete sites; a population of microspheres comprising at least a first and a second sub-population each comprising a bioactive agent; and a fiducial (i.e. marker bead, Column 19, lines 2-5) wherein said microspheres are randomly distributed on said surface such that said discrete sites contain microspheres; using the fiducial to register said first data image to create a registered first data image; contacting said random array with said sample; acquiring a second data image from said array with said sample; using the fiducial to register said second data image to create a registered second data image; and comparing said first and said second registered data images to determine the presence or absence of said target analyte (Column 18, line 59-Column 19, line 62 and Claims 17-21) wherein additional, non-optical signature encoding, is used e.g. size, shape and/or dimension of the microspheres and/or optical fibers (Column 19, lines 6-30) and Brenner et al. who teach a similar array composition comprising microspheres which do not comprise an optical signature and wherein microspheres size and shape are selected based on experimental design (Column 9, lines 62-65; Column 19, line 20-49; and Column 21, line 15-Column 22, line 61). One skilled in the art would have been motivated to modify the microspheres of Walt et al by replacing the optical signature microspheres of one subpopulation with non-labeled

microspheres as taught by Brenner et al to thereby eliminate the need to provide optical signatures on all the microspheres for the obvious benefits of simplicity. Walt et al do not teach at least a first edge of the array is a fiducial edge. However, Augenlicht teaches a similar method for determining the presence of a target comprising a substrate with a surface comprising discrete sites and at least a first and second population each comprising a bioactive agent distributed on the surface; acquiring a data image to create a registered image and comparing registered images to determine the presence of said target wherein the registered image utilizes a fiducial marking (Column 7, lines 18-46) wherein at least a first edge of the array is a fiducial edge i.e. upper right edge, upper left edge and lower left edge (Fig. 1) and wherein the fiducial markings permit rapid and accurate automated scanning to thereby identify targets rapidly and accurately (Column 8, lines 15-29). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the substrate of Walt et al. by utilizing a fiducial edge as suggested by Augenlicht to thereby reduce operator time and human error by permitting automated scanning of the substrate for the expected benefit of rapid and accurate target analysis as suggested by Augenlicht (Column 8, lines 15-29).

Regarding Claim 70, Walt et al teach the array comprises at least three fiducial and each is a fiducial fiber i.e. a unique tag for each of 100 different subarrays (Column 18, line 59-Column 19, line 5) wherein the fiducials have different sizes (Column 19, lines 6-30) but they do not teach the fiducials have different shapes. However, the skilled practitioner in the art would have been further motivated to modify the different sized fiducial markers of Walt et al by providing at least one fiducial having a different shape to thereby obtain a substrate having fiducials of differing and identifiable shape (e.g. a different identifiable shape in each coroner) for the obvious benefit of facilitating identification the target analyte. Because subarrays each having a fiducial of different shape would permit identification of the subarray by simple visual identification of fiducial shape thereby facilitating identification of the subarray and target

analyte. Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the fiducial-containing array of Walt et al by encompassing a fiducial of different shape into each subarray for the obvious benefits of facilitating target analyte identification.

Regarding Claim 75, the array wherein the registration utilizes at least three fiducial and each of said fiducials is a microsphere i.e. marker beads which identify each of 100 subarrays (Column 18, line 57-column 19, line 5) and they also teach the fiducials are identified by size (Column 19, lines 7-12) and therefore the fiducials are not identified by label which suggests that the fiducials are not labeled. However, Walt et al do not specifically teach unlabeled fiducials. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the different-sized fiducials of Walt et al by providing unlabeled fiducials of different size based on the suggestion of Walt et al to thereby eliminate the labeling step for the obvious benefit of convenience and economy of time and labor.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

6. No claim is allowed.

7. The examiner's Art Unit has changed from 1655 to 1634. Please address future correspondence to Art Unit 1634.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
October 9, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600